OUT OF CONTROL

AIDS and the corruption of medical science

By Celia Farber

Joyce Ann Hafford was a single mother living alone with her thirteen-year-old son, Jermal, in Memphis, Tennessee, when she learned that she was pregnant with her second child. She worked as a customer service representative at a company called CMC Call Center; her son was a top student, an athlete and musician. In April 2003, Hafford, four months pregnant, was urged by her obstetrician to take an HIV test. She agreed, even though she was healthy and had no reason to think she might be HIV positive. The test result came up positive, though Hafford was tested only once, and she did not know that pregnancy itself can cause a false positive HIV test. Her first thought was of her unborn baby. Hafford was immediately referred to an HIV/AIDS specialist, Dr. Edwin Thorpe, who happened to be one of the principal investigators recruiting patients for a clinical trial at the University of Tennessee Medical Group that was sponsored by the Division of AIDS (DAIDS)—the chief branch of HIV/AIDS research within the National Institutes of Health.

The objective of the trial, PACTG 1022, was to compare the "treatment-limiting toxicities" of two anti-HIV drug regimens. The core drugs being compared were nelfinavir (trade name Viracept) and nevirapine (trade name Viramune). To that regimen, in each arm, two more drugs were added—zidovudine (AZT) and lamivudine (Epivir) in a branded combination called Combivir. PACTG 1022 was a "safety" trial as well as an efficacy trial, which means that pregnant women were being used as research subjects to investigate "safety" and yet the trial was probing the outer limits of bearable toxicity. Given the reigning beliefs about HIV's pathogenicity, such trials are fairly commonplace, especially in the post-1994 era, when AZT was hailed for cutting transmission rates from mother to child.

The goal of PACTG 1022 was to recruit at least 440 pregnant women across the nation, of which 15 were to be enrolled in the University of Tennessee Medical Group. The plan was to assign the study's participants to one of two groups, with each receiving three HIV drugs, starting as early as ten weeks of gestation. Of the four drugs in this study, three belong to the FDA's category "C," which means that safety to either mother or fetus has not been adequately established.

Joyce Ann Hafford was thirty-three years old and had always been healthy. She showed no signs of any of the clinical markers associated with AIDS—her CD4 counts, which measure the lymphocytes that are used to indicate how strong a person's immune system is, and which HIV is believed to slowly corrode, were in the

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Illustrations by Danijel Zezelj

normal range, and she felt fine. In early June 2003, she was enrolled in the trial and on June 18 took her first doses of the drugs. "She felt very sick right away," recalls her older sister, Rubbie King. "Within seventy-two hours, she had a very bad rash, welts all over her face, hands, and arms. That was the first sign that there was a problem. I told her to call her doctor and she did, but they just told her to put hydrocortisone cream on it. I later learned that a rash is a very bad sign, but they didn't seem alarmed at all."

Hafford was on the drug regimen for thirty-eight days. "Her health started to deteriorate from the moment she went on the drugs," says King. "She was always in pain, constantly throwing up, and finally she got to the point where all she could do was lie down." The sisters kept the news of Hafford's HIV test and of the trial itself from their mother, and Hafford herself attributed her sickness and nausea to being pregnant. She was a cheerful person, a non-complainer, and was convinced that she was lucky to have gotten into this trial. "She said to me, 'Nell' —that's what she called me—'I have got to get through this. I can't let my baby get this virus.' I said, 'Well, I understand that, but you're *awful* sick.' But she never expressed any fear because she thought this was going to keep her baby from being HIV positive. She didn't even know she was in trouble."

On July 16, at her scheduled exam, Hafford's doctor took note of the rash, which was "pruritic and macular-papular," and also noted that she was suffering hyperpigmentation, as well as ongoing nausea, pain, and vomiting. By this time all she could keep down were cans of Ensure. Her blood was drawn for lab tests, but she was not taken off the study drugs, according to legal documents and internal NIH memos.

Eight days later, Hafford went to the Regional Medical Center "fully symptomatic," with what legal documents characterize as including: "yellow eyes, thirst, darkening of her arms, tiredness, and nausea without vomiting." She also had a rapid heartbeat and difficulty breathing. Labs were drawn, and she was sent home, still on the drugs. The next day, July 25, Hafford was summoned back to the hospital after her lab reports from nine days earlier were finally reviewed. She was admitted to the hospital's ICU with "acute and sub-acute necrosis of the liver, secondary to drug toxicity, acute renal failure, anemia, septicemia, premature separation of the placenta," and threatened "premature labor." She was finally taken off the drugs but was already losing consciousness. Hafford's baby, Sterling, was delivered by C-section on July 29, and she remained conscious long enough not to hold him but at least to see him and learn that she'd had a boy. "We joked about it a little, when she was still coming in and out of consciousness in ICU," Rubbie recalls. "I said to her, 'You talked about me so much when you were pregnant that that baby looks *just* like me.'" Hafford's last words were a request to be put on a breathing tube. "She said she thought a breathing tube might help her," says Rubbie. "That was the last conversation I had with my sister." In the early morning hours of August 1, Rubbie and her mother got a call to come to the hospital, because doctors had lost Hafford's pulse. Jermal was sleeping, and Rubbie woke her own daughter and instructed her not to tell Jermal anything yet. They went to the hospital, and had been there about ten minutes when Joyce Ann died.

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Rubbie recalls that the hospital staff said they would clean her up and then let them sit with her. She also remembered a doctor who asked for their home phone numbers and muttered, "You got a lawsuit." (That person has not resurfaced.) They hadn't been sitting with Hafford's body long when a hospital official came in and asked the family whether they wanted an autopsy performed. "We said yes, we sure do," she says. The hospital official said it would have to be at their expense—at a cost of $3,000. "We said, 'We don't have $3,000.' My sister didn't have any life insurance or anything," says Rubbie. "She had state health care coverage, and we were already worried about how to get the money together to bury her." Consequently, no autopsy was done. There was a liver biopsy, however, which revealed, according to internal communiqués of DAIDS staff, that Hafford had died of liver failure brought on by nevirapine toxicity.

And what was the family told about the cause of Hafford's death?

"How did they put it?" Rubbie answers, carefully. "They told us how safe the drug was, they never attributed her death to the drug itself, at all. They said that her disease, AIDS, must have progressed rapidly." But Joyce Ann Hafford never had AIDS, or anything even on the diagnostic scale of AIDS. "I told my mom when we were walking out of there that morning," Rubbie recalls, "I said, 'Something is wrong.' She said, 'What do you mean?' I said, 'On the one hand they're telling us this drug is so safe, on the other hand they're telling us they're going to monitor the other patients more closely. If her disease was progressing, they could have changed the medication.' I knew something was wrong with their story, but I just could not put my finger on what it was."

When they got home that morning, they broke the news to Jermal. "I think he cried the whole day when we told him," Rubbie recalls. "My mom had tried to prepare him. She said, 'You know, Jermal, my mom died when I was very young,' but he was just devastated. They were like two peas in a pod those two. You could never separate them." Later on, Jermal became consumed with worry about how they would bury his mother, for which they had no funds and no insurance. The community pitched in, and Hafford was buried. "I haven't even been able to go back to her grave since she passed," says Rubbie.

Rubbie King is haunted by many questions, including whether her sister

was really infected with HIV,[1] and also what the long-term damage might be to Sterling, whom Rubbie is now raising, along with Jermal and her own child. Sterling, in addition to the drugs he was exposed to in the womb, was also on an eight-week AZT regimen after birth. One of the reasons the family suspects Hafford may have been a false positive is that St. Jude's Children's Research Hospital has not released Sterling's medical records, and although they have been told that he is now HIV negative, they never had any evidence that he was even born positive. (All babies born to an HIV-positive mother are born positive, but most become negative within eighteen months.)

Hafford's family was never told that she died of nevirapine toxicity. "They never said that. We never knew what she had died of until we got the call from [AP reporter] John Solomon, and he sent us the report," says Rubbie King. "It was easier to accept that she died of a lethal disease. That was easier to handle." The family has filed a $10 million lawsuit against the doctors who treated Hafford, the Tennessee Medical Group, St. Jude's Children's Research Hospital, and Boehringer Ingelheim, the drug's manufacturer.[2]

Rubbie King made a final, disturbing discovery when she was going through Hafford's medical records: In addition to discovering that her sister had only ever been given a single HIV test, she also came across the fifteen-page consent form, which was unsigned.

On August 8, 2003, Jonathan Fishbein, who had recently taken a job as the director of the Office for Policy in Clinical Research Operations at DAIDS, wrote an email to his boss, DAIDS director Ed Tramont, alerting him that "there was a fulminant liver failure resulting in death" in a DAIDS trial and that it looked like "nevirapine was the likely culprit." He said that the FDA was being informed. He was referring to Joyce Ann Hafford. Tramont emailed him back, "Ouch. Not much wwe can do about dumd docs!"

This email exchange came to light in December 2004, when AP reporter John Solomon broke the story that Fishbein was seeking whistle-blower protection, in part because he had refused to sign off on the reprimand of an NIH officer who had sent the FDA a safety report concerning the DAIDS trial that launched the worldwide use of nevirapine for pregnant women. The study was called HIVNET 012, and it began in Uganda in 1997.

The internal communiqués from DAIDS around the time of Hafford's death made it clear that doctors knew she had died of nevirapine toxicity. Tramont's reply to Fishbein suggests that he thought blame could be placed squarely with Hafford's doctors, but it

[1] *HIV tests detect footprints, never the animal itself. These footprints, antibodies, are identified by means of molecular protein weights, and were limited to two in 1984, when the first test was developed and patented, but over the years expanded to include many proteins previously not associated with HIV. Like most Americans, Hafford thought that a single HIV-positive test meant that she "had" HIV—a surefire death sentence. But a majority of HIV-positive tests, when retested, come back indeterminate or negative. In many cases, different results emerge from the same blood tested in different labs. There are currently at least eleven different criteria for how many and what proteins at which band density signal "positive." The most stringent criteria (four bands) are upheld in Australia and France; the least stringent (two bands), in Africa, where an HIV test is not even required as part of an AIDS diagnosis. The U.S. standard is three reactive bands. It has been pointed out that a person could revert to being HIV negative simply by buying a plane ticket from Uganda to Australia.*

[2] *Dr. Thorpe declined to comment, citing ongoing litigation, as did the Tennessee Medical Group, the Regional Medical Center at Memphis, and St. Jude's Children's Research Hospital.*

was the NIH itself that had conceived of the study as one that tested the "treatment-limiting toxicities" of HIV drugs in pregnant women.

The conclusion of the PACTG 1022 study team was published in the journal *JAIDS* in July of 2004. "The study was suspended," the authors reported, "because of greater than expected toxicity and changes in nevirapine prescribing information." They reported that within the nevirapine group, "one subject developed fulminant hepatic liver failure and died, and another developed Stevens-Johnson syndrome." Stevens-Johnson syndrome is skin necrolysis—a severe toxic reaction that is similar to internal third-degree burns, in which the skin detaches from the body. Another paper, entitled "Toxicity with Continuous Nevirapine in Pregnancy: Results from PACTG 1022," puts the results in charts, with artful graphics. A small illustration of Hafford's liver floats in a box, with what looks like a jagged gash running through it. Four of the women in the nevirapine group developed hepatic toxicity.

As Terri Schiavo lay in her fourteenth year of a persistent vegetative state, and the nation erupted into a classically American moral opera over the sanctity of life, Joyce Ann Hafford's story made only a fleeting appearance—accompanied by a photo of her holding a red rose in an article that was also written by the AP's John Solomon. But soon a chorus of condemnation was turned against those who were sensationalizing Hafford's death and the growing HIVNET controversy to condemn nevirapine, which had been branded by the AIDS industry as a "life-saving" drug and a "very important tool" to combat HIV in the Third World.

So-called community AIDS activists were sprung like cuckoo birds from grandfather clocks at the appointed hour to affirm the unwavering AIDS cathechism: AIDS drugs save lives. To suggest otherwise is to endanger millions of African babies. Front and center were organizations like the Elizabeth Glaser Pediatric AIDS Foundation, which extolled the importance of nevirapine. Elizabeth Glaser's nevirapine defenders apparently didn't encounter a single media professional who knew, or cared, that the organization had received $1 million from nevirapine's maker, Boehringer Ingelheim, in 2000.[3] This was no scandal but simply part of a landscape. Pharmaceutical companies fund AIDS organizations, which in turn are quoted uncritically in the media about how many lives their drugs save. This time the AIDS organizations were joined by none other than the White House, which was in the midst of promoting a major program to make nevirapine available across Africa.[4]

America is a place where people rarely say: *Stop*. Extreme and unnatural things happen all the time, and nobody seems to know how to hit the brakes. In this muscular, can-do era, we are particularly prone to the seductions of the pharmaceutical industry, which has successfully marketed its ever growing arsenal of drugs as the latest American *right*. The buzzword is "access,"

[3] *"Our mission of eradicating AIDS is always informed and driven by the best available science, not by donations," said Mark Isaac, Elizabeth Glazer's vice president for policy, when asked to comment. "The full body of research, as well as our extensive experience, validates the safety and efficacy of single-dose nevirapine as one of several options to prevent mother-to-child transmission of HIV."*

[4] *Africa, as the news media never tires of telling us, has become ground zero of the AIDS epidemic. The clinical definition of AIDS in Africa, however, is stunningly broad and generic, and was seemingly designed to be little other than a signal for funding. It is in no way comparable to Western definitions. The "Bangui definition" of AIDS was established in the city of Bangui in the Central African Republic, at a conference in 1985. The definition requires neither a positive HIV test nor a low T-cell count, as in the West, but only the presence of chronic diarrhea, fever, significant weight loss, and asthenia, as well as other minor symptoms. These happen to be the symptoms of chronic malnutrition, malaria, parasitic infections, and other common African illnesses. (In 1994 the definition was updated to suggest the use of HIV tests, but in practice they are prohibitively expensive.) Even when HIV tests are performed, many diseases that are endemic to Africa, such as malaria and TB, are known to cause false positives. The statistical picture of AIDS in Africa, consequently, is a communal projection based on very rough estimates of HIV positives, culled from select and small samples, which are extrapolated across the continent using computer models and highly questionable assumptions.*

which has the advantage of short-circuiting the question of whether the drugs actually work, and of utterly obviating the question of whether they are even remotely safe. This situation has had particularly tragic ramifications on the border between the class of Americans with good health insurance, who are essentially consumers of pharmaceutical goods, and those without insurance, some of whom get drugs "free" but with a significant caveat attached: They agree to be experimented on. These people, known in the industry as "recruits," are pulled in via doctors straight from clinics and even recruited on the Internet into the pharmaceutical industry and the government's web of clinical trials, thousands of which have popped up in recent years across the nation and around the world. Such studies help maintain the industry's carefully cultivated image of benign concern, of charity and progress, while at the same time feeding the experimental factories from which new blockbuster drugs emerge. "I call them what they are: human experiments," says Vera Hassner Sharav, of the Alliance for Human Research Protection in New York City. "What's happened over the last ten to fifteen years is that profits in medicine shifted from patient care to clinical trials, which is a *huge* industry now. Everybody involved, except the subject, makes money on it, like a food chain. At the center of it is the NIH, which quietly, while people weren't looking, wound up becoming the partner of industry."

By June 2004, the National Institutes of Health had registered 10,906 clinical trials in ninety countries. The size of these trials, which range from the hundreds to more than 10,000 people for a single study, creates a huge market for trial participants, who are motivated by different factors in different societies but generally by some combination of the promise of better health care, prenatal care, free "access" to drugs, and often—especially in the United States—cash payments. Participating doctors, whose patient-care profits have been dwindling in recent years because of insurance-company restrictions, beef up their incomes by recruiting patients.

Dr. Jonathan Fishbein is hardly a rabble-rouser. But he is a passionate advocate of "good clinical practice," or GCP, a set of international standards that were adopted in 1996, as clinical-trial research boomed. The GCP handbook states: "Compliance with this standard provides public assurance that the rights, safety, and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible." During the decade prior to his arrival at DAIDS, Fishbein had overseen and consulted on hundreds of clinical trials for just about every pharmaceutical company. Fishbein knew, before he took his job as director of the Office for Policy in Clinical Research Operations at DAIDS, that there was a troubled study haunting the whole division. Nobody was supposed to talk about it, but it hung heavily in the air. "Something about Uganda, that's all I knew," he says. There was a trial staged there, a big one, that had been plagued with "problems," and there was also a lot of talk about one particular employee connected to this trial who would need to be disciplined. Soon he discovered just how bad the situation was. "The HIVNET thing," he recalls, "it hit me like a fire hose when I walked in there."

FISHBEIN KNEW THAT A TROUBLED STUDY WAS HAUNTING DAIDS. "SOMETHING ABOUT UGANDA, THAT'S ALL I KNEW"

Fishbein's position was new. "It sounded like a very important position," he says. "I was to oversee the policies governing all the clinical-research operations, both here and abroad." He was told he would have "go–no go" authority over individual trials. It wasn't long before Fishbein realized that he was, in effect, taking a job that was the equivalent of piloting an already airborne plane. "They had all these trials going on, and hundreds of millions of dollars flowing in every year, but there was apparently no one in a senior position there who really had clinical expertise—who knew all the nuances, rules, and regulations in the day-to-day running of clinical trials." DAIDS, when Fishbein came to work there in 2003, was running about 400 experimental trials both in the United States and abroad.

A DAIDS project officer close to the HIVNET study closed the door when she had her first meeting with Fishbein. She had also crossed over from the private sector, and so she and Fishbein shared a disillusionment over how much shoddier and more chaotic the research culture was within the government, compared with industry. "I'm really frightened about the stuff that goes on here," she told him. "We really need somebody." This project officer, who for her own protection cannot be named, told Fishbein that the division's flagship study in Africa—HIVNET 012—had been wracked with problems and completely lacking in regulatory standards. She told Fishbein that the trial investigators were "out of control," and that there was no oversight of them, and nobody with either the inclination or the authority to make them adhere to safety standards. What Fishbein subsequently learned entangled him in a story with eerie echoes of John Le Carré's *Constant Gardener*.

For our purposes, the story of nevirapine begins in 1996, when the German pharmaceutical giant Boehringer Ingelheim applied for approval of the drug in Canada. The drug had been in development since the early 1990s, which was a boom time for new HIV drugs. Canada rejected nevirapine twice, once in 1996 and again in 1998, after the drug showed no effect on so-called surrogate markers (HIV viral load and CD4 counts) and was alarmingly toxic. In 1996, in the United States, the FDA nonetheless gave the drug conditional approval so that it could

be used in combination with other HIV drugs.[5]

By this time, Johns Hopkins AIDS researcher Brooks Jackson had already generated major funding from the NIH to stage a large trial for nevirapine in Kampala, Uganda, where the benevolent dictator Yoweri Museveni had opened his country to the lucrative promise of AIDS drug research, as well as other kinds of pharmaceutically funded medical research. HIVNET 012, according to its original 1997 protocol, was intended to be a four-arm, Phase III, randomized, placebo-controlled trial.[6] Its sole sponsor was listed as the National Institute of Allergy and Infectious Diseases (NIAID), though one of the investigators was a Boehringer employee. The "sample size" was to be 1,500 HIV-1 infected Ugandan women more than thirty-two weeks pregnant. The four arms they would be divided into were 1) A single dose of 200mg nevirapine at onset of labor and a single 2mg dose to the infant forty-eight to seventy-two hours post-delivery, and 2) a corresponding placebo group; 3) 600mg of AZT at onset of labor and 300mg until delivery, with a 4mg AZT dose for the infant lasting seven days after birth, and 4) a corresponding placebo group. There were to be 500 women in each "active agent" arm and 250 in each placebo arm. The study was to last eighteen months, and its "primary endpoints" were to see how these two regimens would affect rates of HIV transmission from mother to child, and to examine the "proportion of infants who are alive and free of HIV at 18 months of age." Another primary objective was to test the "safety/tolerance" of nevirapine and AZT. HIVNET's architects estimated that more than 4,200 HIV-positive pregnant women would deliver at Mulago hospital each year, allowing them to enroll eighty to eighty-five women per month. Consent forms were to be signed by either the mother or a guardian, by signature or "mark." One of the exclusion criteria was "participation during current pregnancy in any other therapeutic or vaccine perinatal trial."

Although HIVNET was designed to be a randomized, placebo-controlled, double-blind, Phase III trial of 1,500 mother/infant pairs, it wound up being a no-placebo, neither double- nor even single-blind Phase II trial of 626 mother/infant pairs. Virtually all of the parameters outlined for HIVNET 012 were eventually shifted, amended, or done away with altogether, beginning with perhaps the most important—the placebo controls. By a "Letter of Amendment" dated March 9, 1998, the placebo-control arms of HIVNET were eliminated. The study as reconstituted thus amounted to a simple comparison of AZT and nevirapine.

On September 4, 1999, *The Lancet* published HIVNET's preliminary results, reporting that "Nevirapine lowered the risk of HIV-I transmission during the first 14–16 weeks of life by nearly 50 percent." The report concluded that "the two regimens were well-tolerated and adverse events were similar in the two groups." The article also reported that thirty-eight babies had died, sixteen in the nevirapine group and twenty-two in the AZT group. The rate of HIV transmission in the AZT arm was 25 percent, while in the nevirapine group it was only 13 percent. As *Hopkins Medical News* later reported, the study was received rapturously. "The data proved stunning. It showed that nevirapine was 47 percent more effective than AZT and had reduced the number of infected infants from 25 to 13 percent. Best of all, nevirapine was inexpensive—just $4 for both doses. If implemented widely, the drug could prevent HIV transmission in more than 300,000 newborns a year."

With the results of the study now published in *The Lancet*, Boehringer, which previously had shown little interest in HIVNET, now pressed for FDA approval to have nevirapine licensed for use in preventing the transmission of HIV in pregnancy.

There were complications, however. On December 6, 2000, a research letter in *The Journal of the American Medical Association* warned against using nevirapine for post-exposure treatment after two cases of life-threatening liver toxicity were reported among health-care workers who'd taken the drug for only a few days. (One of them required a liver transplant.) The January 5, 2001, issue of the CDC's *Morbidity and Mortality Weekly Report* (*MMWR*) contained an FDA review of MedWatch—an informal reporting system of drug reactions—that highlighted an additional twenty cases of "serious adverse events" resulting from fairly brief nevirapine post-exposure prophylaxis. "Serious adverse events" were defined as anything "life-threatening,

[5] *Asked to comment about the Hafford case, HIVNET 012, and the larger nevirapine controversy, Boehringer Ingelheim provided the following statement: "Viramune ® (nevirapine) was an innovation in anti-HIV treatment as the first member of the non-nucleoside reverse transcriptase inhibitor (NNRTI) class of drugs. Now in its tenth year of use, Viramune has been used as a treatment in more than 800,000 patient-years worldwide."*

[6] *The study was originally titled "HIVNET 012: A Phase III Placebo-Controlled Trial to Determine the Efficacy of Oral AZT and the Efficacy of Oral Nevirapine for the Prevention of Vertical Transmission of HIV-1 Infection in Pregnant Ugandan Women and Their Neonates." "Randomization" means that people are randomly chosen for one arm of the study or another, a procedure that is supposed to even out the variables that could affect the outcome. "Placebo controls" are the bedrock of drug testing and are the only way to know whether the treatment is effective. Phase I trials involve a small group of people, twenty to eighty, and are focused on safety and side effects. In Phase II trials the drug is given to an expanded cohort, between 100 and 300, to further evaluate safety and begin to study effectiveness. Phase III drug trials expand further the number of people enrolled, often to more than 1,000, and are meant to confirm a drug's effectiveness, monitor side effects, and compare it with other treatments commonly used. A small Phase I trial preceded HIVNET 012 that studied the safety, primarily, of nevirapine in pregnant women but also looked at efficacy. It was called HIVNET 006, and it enrolled twenty-one pregnant women for initial study. Of twenty-two infants born, four died. There were twelve "serious adverse events" reported. The study also showed that there was no lowering of viral load in the mothers who took the study drug (the industry's agreed-upon standard for interrupting maternal transmission).*

permanently disabling," or requiring "prolonged hospitalization, or [. . .]intervention to prevent permanent impairment or damage." The *MMWR* stressed that there probably were more unreported cases, since the reporting by doctors to MedWatch is "voluntary" and "passive."

But NIAID was on another track altogether, either oblivious of or undeterred by the toxicity controversy. In 2001, Boehringer Ingelheim submitted its supplemental licensing request to the FDA. The request was submitted based entirely on the results of HIVNET, as published in *The Lancet*. Around the same time, the South African Medicines Control Counsel (MCC) conditionally approved nevirapine for experimental use in mother-to-child transmission treatment. To its credit, however, the FDA decided to go to Kampala, inspect the site, and review the data itself.

Since Boehringer had not originally intended to use this study for licensing purposes, it decided to perform its own inspection before the FDA arrived. Boehringer's team arrived in Kampala and did a sample audit. They were the first to discover what a shambles the study was. According to Boehringer's preinspection report, "serious non-compliance with FDA Regulations was found" in the specific requirements of reporting serious adverse events. Problems also were found in the management of the trial drug and in informed-consent procedures. DAIDS then hired a private contractor, a company named Westat, to go to Uganda and do another preinspection. This time the findings were even more alarming. One of the main problems was a "loss of critical records." One of two master logs that included follow-up data on adverse events, including deaths, was said to be missing as the result of a flood. The records failed to make clear which mothers had gotten which drug, when they'd gotten it, or even whether they were still alive at various follow-up points after the study. Drugs were given to the wrong babies, documents were altered, and there was infrequent follow-up, even though one third of the mothers were marked "abnormal" in their charts at discharge. The infants that did receive follow-up care were in many cases small and underweight for their age. "It was thought to be likely that some, perhaps many, of these infants had serious health problems." The Westat auditors looked at a sample of forty-three such infants, and all forty-three had "adverse events" at twelve months. Of these, only eleven were said to be HIV positive. The HIVNET team had essentially downgraded all serious adverse events several notches on a scale it had created to adapt to "local" standards. That downgrade meant, among other things, that even seemingly "life-threatening" events were logged as not serious. Deaths, unless they occurred within a certain time frame at the beginning of the study, were not reported or were listed as "serious adverse events" rather than deaths. In one case, "a still birth was reported as a Grade 3 adverse event for the mother."

As a defense, the HIVNET team often cited ignorance. They told the Westat monitors that they were unaware of safety-reporting regulations, that they'd had no training in Good Clinical Practice, and that they had "never attempted a Phase III trial." The principal investigators and sub-investigators "all acknowledged the findings [of the audit] as generally correct," the Westat report said. "Dr. Guay and Dr. Jackson noted that many ('thousands') of unreported AE's and SAE's occurred. . . . They acknowledged their use of their own interpretation of 'serious' and of severity." "All agreed" that the principal and subinvestigators "had generally not seen the trial patients," and "all agreed" that in evaluating adverse and serious adverse events "they had relied almost entirely on second or third hand summaries . . . without attempting to verify accuracy." Westat also discovered that half the HIV-positive infants were also enrolled in a vitamin A trial, which effectively invalidates any data associated with them.

In light of the Westat report, DAIDS and Boehringer asked the FDA for a postponement of its inspection visit. The FDA responded by demanding to see the report immediately. On March 14, 2002, the FDA called a meeting with DAIDS, Boehringer, and the trial investigators. "They reprimanded the whole gang," says Fishbein. Then they said to Boehringer: Withdraw your application for extended approval, if you want to avoid a public rejection." Boehringer complied with the FDA's demand, though statements put out by NIAID made it sound as if the company had withdrawn the application for FDA approval in a spirit of profound concern for protocol. In South Africa, a few months later, the news focused on

the angry chorus of AIDS experts and activists, speaking as one. The South African MCC was reconsidering its approval of nevirapine for pregnant women because of Boehringer's withdrawal and the growing HIVNET controversy. The Associated Press reported that "activists fear the government, notorious for its sluggish response to the AIDS crisis, is pressuring the council to reject nevirapine, and that it could misrepresent the current discussions as proof the drug is toxic. Studies show nevirapine given to HIV-pregnant women during labor and to their newborn babies can reduce HIV transmission by up to 50 percent." The problem with such statements, of course, is that the study in question was precisely the one that established the claim that nevirapine cut HIV transmission.

Two inspections had now declared HIVNET to be a complete mess: Boehringer's own and Westat's, which had been performed in conjunction with DAIDS. But the ways in which the various players were tethered together made it impossible for DAIDS to condemn the study without condemning itself.[7] But DAIDS was well aware of what had transpired.

According to DAIDS's public version of events, which was dutifully echoed in the AIDS press, the trouble with HIVNET was that it was unfairly assailed by pedantic saboteurs who could not grasp the necessary difference between U.S. safety standards and the more lenient standards that a country like Uganda deserved. Two weeks after the fifty-seven-page Westat report was delivered, the deputy director of NIAID, Dr. John LaMontagne, had set the tone by stating publicly: "There is no question about the validity [of the HIVNET results]...the problems are in the rather arcane requirements in record keeping." DAIDS was so dismissive of the Westat report that Westat's lawyers eventually put officials on notice that they were impugning Westat's reputation.

Meanwhile, as the investigations continued, nevirapine had long since been recommended by the World Health Organization and registered in at least fifty-three countries, and Boehringer had begun shipping boxes of the drug to maternity wards across the developing world. In 2002, President Bush announced a $500 million program to prevent maternal transmission of HIV in which nevirapine therapy would play a major role—despite the fact that the drug has never received FDA approval for this purpose.

TWO INSPECTIONS HAD NOW DECLARED HIVNET TO BE A COMPLETE MESS: BOEHRINGER'S OWN AND WESTAT'S

In 2003, when Jonathan Fishbein was drawn into the HIVNET saga, the cover-up (for that, ultimately, is what the NIH response had become) was ongoing. In response to the massive failures documented by Boehringer and Westat, DAIDS embarked on a "remonitoring review" in an attempt to validate the study's results. Ordinarily, an outside contractor would be retained for such a complex project, but Tramont made the decision to keep the remonitoring in-house. Drafting the review was a massive undertaking that took months of research, lengthy interviews with the investigators, and painstaking analysis of poorly organized documentation, as the DAIDS team attempted to learn what had actually taken place in Kampala. Even so, Tramont wanted the HIVNET site reopened in time for President Bush's visit to Uganda. In March 2003, Tramont and his staff gathered together the different sections and substantially rewrote the report, especially the safety section, minimizing the toxicities, deaths, and record-keeping problems. The rewritten report concluded that nevirapine was safe and effective for the treatment of mother-to-child transmission of HIV, thus saving HIVNET 012 from the scrapheap of failed scientific studies.

While preparing the safety review section, however, an NIH medical officer named Betsy Smith noticed a pattern of elevated liver counts among some of the babies in the AZT arm. Following FDA regulations, she drafted a safety report documenting this finding and gave it to Mary Anne Luzar, a DAIDS regulatory affairs branch chief. Luzar forwarded the safety report to the FDA. The HIVNET investigators were furious; Tramont, who had previously signed off on the safety report, ordered a new version to be drafted, essentially retracting the previous one, and sent it to the FDA.[8] The political stakes were very high: nevirapine was now a major element in the Administration's new $15 billion African AIDS program—on July 11, President Bush even toured the HIVNET site in Kampala, which DAIDS had reopened for the occasion over Fishbein's objections.

By late June 2003, Jonathan Kagan, the deputy director of DAIDS, asked Fishbein to sign off on a reprimand of Luzar for insubordination. Fishbein reviewed the HIVNET documentation and concluded that Luzar had done nothing wrong, that she had simply followed protocol. Fishbein's refusal to go along with Luzar's reprimand amounted to a refusal to participate in the HIVNET cover-up. In July, Tramont sent an email to all DAIDS staff instructing them not to speak about HIVNET at all. "HIVNET 012 has

[7] *Brooks Jackson declined to comment for this article. Laura Guay responded with the following statement: "Several in-depth reviews of the conduct and results of the HIVNET 012 trial as well as the data collected from subsequent trials and PMTCT programs, have substantiated the HIVNET 012 conclusions that Nevirapine is safe and effective in preventing mother-to-child HIV transmission. Nevirapine remains one of the most important tools for the prevention of mother-to-child HIV transmission in the developing world, where there are still hundreds of thousands of HIV-infected pregnant women who do not have access to any HIV testing, antiretroviral therapy, or HIV care at all. For many programs struggling to establish PMTCT programs with limited resources, Nevirapine is often the only option available." Family Health International, the NIH contractor originally responsible for monitoring HIVNET 012, contested the Westat report and said that the results of the study had been validated by the NIH and the Institute of Medicine.*

[8] *Smith and Luzar have been forbidden by the NIH to speak to the press about HIVNET. Luzar was deposed by Fishbein's attorney in his wrongful-termination lawsuit, Stephen Kohn, in December 2004, and this account is partially based on her deposition.*

been reviewed, re-monitored, debated and scrutinized. To do any more would be beyond reason. It is time to put it behind us and move on. Henceforth, all questions, issues and inquiries regarding HIVNET 012 is [sic] to be referred to the Director, DAIDS."[9]

What followed, as internal emails and memorandums clearly show, was a vicious and personal campaign on the part of Kagan and Tramont to terminate Fishbein's employment. DAIDS officials wrote emails in which they worried about how to fire him without creating repercussions for NIAID director Anthony Fauci, who had given Fishbein a commendation for his work. The communiqués took on conspiratorial tones as Tramont led the operation and mapped out its challenges. On February 23, 2004, Tramont emailed Kagan: "Jon, Let's start working on this—Tony [Fauci] will not want anything to come back on us, so we are going to have to have iron-clad documentation, no sense of harassment or unfairness and, like other personnel actions, this is going to take some work. In Clauswitzian style, we must overwhelm with 'force.' We will prepare our paper work, then . . . go from there." The web now included several more NIH/NIAID employees, who weighed in with suggestions about how best to expel Fishbein without leaving damning legal fingerprints on the proceedings.

Fishbein spent months trying to get a fair hearing, petitioning everyone from Elias Zerhouni, the director of the NIH, to Secretary of Health Tommy Thompson. It was around this time that Fishbein became a "ghost." Nobody addressed him in the corridors, in the elevators, in the cafeteria. "There was an active campaign to humiliate me," he says. "It was as if I had AIDS in the early days. I was like Tom Hanks in *Philadelphia*. Nobody would come near me."

In March 2004, Fishbein began seeking whistle-blower protection. He met with congressional staff and attracted enough attention on Capitol Hill to force the NIH to agree to a study by the National Academy's Institute of Medicine (IOM). The terms of that inquiry were skewed from the outset, however, and the nine-member panel decreed that it would not deal with any questions of misconduct. The panel ignored Fishbein's evidence that DAIDS had covered up the study's failures and relied on testimony from the HIVNET investigators and NIH officials. Not surprisingly, it found that HIVNET's conclusions were valid. Six of the nine members on the panel were NIH grant recipients, with yearly grants ranging from $120,000 to almost $2 million.[10]

THE QUESTION SHOULD NOT BE, IS NEVIRAPINE BETTER THAN AZT? BUT, IS NEVIRAPINE BETTER THAN NOTHING?

Fishbein dismissed the IOM report as a whitewash. Indeed, the report's conclusions are hard to credit, given the overwhelming evidence uncovered by the Westat investigation and documentation such as the following email, which was sent by Jonathan Kagan to Ed Tramont on June 19, 2003. Tramont was considering HIVNET researchers Jackson and Guay for an award:

> Ed—I've been meaning to respond on this—the bit about the award. I think that's a bit over the top. I think that before we start heaping praise on them we should wait to see if the lessons stick. We cannot lose sight of the fact that they screwed up big time. And you bailed their asses out. I'm all for forgiveness, etc. I'm not for punishing them. But it would be "over the top" to me, to be proclaiming them as heroes. Something to think about before pushing this award thing . . .

NIAID has issued a total ban against any employee speaking to the press about Fishbein's allegations. Instead, they have posted "Questions and Answers" about the matter on their website. The first question is: "Is single-dose nevirapine a safe and effective drug for the prevention of mother-to-infant transmission of HIV?" Fishbein has said that due to the spectacular failures of the HIVNET trial, the answer to this is not known, and not knowable. Fishbein believes that ultimately the HIVNET affair is not "about" nevirapine or even AIDS, but about the conduct of the federal government, which has been entrusted to do research on human beings and to uphold basic standards of clinical safety and accuracy.

NIAID answers its first question mechanically and predictably: "Single-dose nevirapine is a safe and effective drug for preventing mother-to-infant transmission of HIV. This has been proven by multiple studies, including the HIVNET 012 study conducted in Uganda." The phrase "safe and effective" has been baked into both the question and the answer, rendering both blank and devoid of meaning. The "multiple studies" line is a familiar tactic, designed to deflect from the study that is actually being addressed, and that is HIVNET 012.

A short letter published in the March 10, 2005, issue of *Nature* quietly unpegged the core claim of NIAID and its satellite organizations in the AIDS industry regarding nevirapine's "effectiveness." Written by Dr. Valendar Turner, a surgeon at the Department of Health in Perth, Australia, the letter read:

> Sir—While raising concerns about "standards of record keeping" in the HIVNET 012 trial in Uganda, in your News story, "Activists and Researchers rally behind AIDS drug for mothers," you overlook a greater flaw. None of the available evidence for nevirapine comes from a trial in which it was tested against a placebo. Yet, as the study's senior author has said, a placebo is the only way a scientist can assess a drug's effectiveness with scientific certainty.

[9] *At this point the story grows ever more complicated, as Fishbein supported Luzar in a sexual-harassment claim against Kagan.*

[10] *An internal NIH investigation, which was obtained by the Associated Press last summer, vindicated many of Fishbein's charges and concluded that "it is clear that DAIDS is a troubled organization," and that the Fishbein case "is clearly a sketch of a deeper issue." Kagan and Tramont did not return repeated calls for comment. Instead, an NIH spokesman, Dr. Cliff Lane, said that the agency stands by HIVNET 012.*

The HIVNET 012 trial abandoned its placebo group in early 1998 after only 19 of the 645 mothers randomized had been treated, under pressure of complaints that the use of a placebo was unethical.

The HIV transmission rate reported for nevirapine in the HIVNET 012 study was 13.1%. However, without antiviral treatments, mother-to-child transmission rates vary from 12% to 48%. The HIVNET 012 outcome is higher than the 12% transmission rate reported in a prospective study of 561 African women given no antiretroviral treatment.

The letter concluded by asking: "On what basis can it be claimed that 'there's nothing that has in any way invalidated the conclusion that single-dose nevirapine is effective for reducing mother-to-child transmission'? Without supporting evidence from a placebo-controlled randomized trial, such statements seem unwarranted." HIVNET claimed to reduce HIV transmission by "nearly 50 percent" by comparing a nevirapine arm to an AZT arm. Turner's letter points out that 561 African women taking no antivirals transmitted HIV at a rate of 12 percent. Had nevirapine been asked to compete with that placebo group, it would have lost. As it was, there was no placebo group, so HIVNET's results are a statistical trick, a shadow play, in which success is measured against another drug and not against a placebo group—the gold standard of clinical trials. The question should not be, Is nevirapine better than AZT? but, *Is nevirapine better than nothing?*

Independent evidence suggests that it is not.

A 1994 study, for example, that gave vitamin A to pregnant HIV-positive mothers in Malawi reported that those with the highest levels of Vitamin A transmitted HIV at a rate of only 7.2 percent. This is consistent with a vast body of research linking nutritional status to sero-conversion, as well as to general health. Another study on the efficacy of nevirapine in mother-to-child transmission was performed by researchers from Ghent University (Belgium) in Kenya and published in 2004.

Dr. Ann Quaghebeur, who led the Ghent study, was reached at her home near London. I asked her what she thought of the reaction to HIVNET 012. She replied in a very quiet voice, almost a whisper. "Our results showed that nevirapine had little effect. I actually felt it was a waste of resources. HIVNET was just one study, but usually before you apply it in a field setting there should be a few more studies to see if it works in real life. What I think they should have done is wait for more studies before they launched this in all those countries." When I asked her how she explained this, she replied, "Well, I want to be careful, there seems to be an industry now."

The failure of the HIVNET researchers to properly control their study with a placebo group is not as unusual as one might think. In fact, this failure is perhaps the outstanding characteristic of AIDS research in general. The 1986 Phase II trial that preceded the FDA's unprecedented rapid approval of AZT was presented as a double-blind, placebo-controlled study, though it was anything but that. As became clear afterward through the efforts of a few journalists, as well as the testimony of participants, the trial was "unblinded" almost immediately because of the severe toxicity of the drug. Members of the control group began to acquire AZT independently or from other study participants, and eventually the study was aborted and everyone was put on the drug. As in the case of HIVNET, documents obtained by journalist John Lauritsen under the Freedom of Information Act subsequently suggested that data-tampering was widespread. Documents were altered, causes of death were unverified, and the researchers tended to assume what they wished to prove, i.e., that placebo-group diseases were AIDS-related but that those in the AZT group were not. So serious were the deviations from experimental protocol at one Boston hospital that an FDA inspector attempted to exclude data from that center. In the end, however, all the data were included in the results, and

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the FDA approved the drug in 1987.[11]

AZT was approved in record time, but that record didn't stand for long. In 1991, the FDA approved another DNA chain terminator, ddI, without even the pretense of a controlled study. Anti-HIV drugs such as Crixivan were approved in as little as six weeks, and cast as a triumph of AIDS activism. This pattern of jettisoning standard experimental controls has continued up to the present, as the HIVNET affair amply demonstrates, and has characterized not only research into new drugs designed to exterminate HIV but the more fundamental questions at the root of AIDS research.

The HIVNET cover-up can only be understood within the larger political context of AIDS. The emergence of this syndrome in the 1980s sparked a medical state of emergency in which scientific controls, the rules that are supposed to bracket the emotions and desires of individual researchers, were frequently compromised or removed entirely. AIDS helped turn disease into politics, and politics, at least in the United States, is all about turning power into money.

No one has been more persistent in calling attention to the failings of AIDS research than Peter Duesberg, a virologist and cancer specialist at the University of California at Berkeley. If Duesberg's name sounds familiar, it's because he has been quite effectively branded in the international media as the virologist who is wrong about HIV. His name entered the popular culture in the late 1980s pre-stamped with wrongness. You knew he was wrong before you knew what he had said in the first place.

In 1987, Duesberg published a paper in the journal *Cancer Research* entitled "Retroviruses as Carcinogens and Pathogens: Expectations and Reality." He was, at the time, at the top of the field of retrovirology, having mapped the genetic structure of retroviruses and defined the first cancer gene in the 1970s. He was the youngest member, at age fifty, ever elected into the National Academy of Sciences. In this paper, which in the words of his scientific biographer, Harvey Bialy, "sealed his scientific fate for a dozen years," Duesberg argued that retroviruses don't cause cancer and concluded by detailing how and why the retrovirus HIV cannot cause AIDS.

As AIDS grew in the 1980s into a global, multibillion-dollar juggernaut of diagnostics, drugs, and activist organizations, whose sole target in the fight against AIDS was HIV, condemning Duesberg became part of the moral crusade. Prior to that 1987 paper, Duesberg was one of a handful of the most highly funded and prized scientists in the country. Subsequently, his NIH funding was terminated and he has received not one single federal research dollar since his pre-1987 Outstanding Investigator Grant ran out. Duesberg lost his lab facilities and had to move twice within a few years to smaller labs on the Berkeley campus, where he spent much of his time writing futile research grant proposals asking to test his hypothesis that AIDS is a chemical syndrome, caused by accumulated toxins from heavy drug use. He lost his graduate students, who were warned that to emerge from his lab would blight their careers. He was denied and had to fight for routine pay increases by his employers at UC Berkeley, where he has tenure and still teaches. He was "dis-invited" from scientific conferences, and colleagues even declared that they would refuse to attend any conference that included him. Duesberg also was banished from publishing in scientific journals that previously had welcomed his contributions, most theatrically by the editor of *Nature*, Sir John Maddox, who wrote a bizarre editorial declaring that Duesberg would be de-

[11] *AZT, which was developed as a chemotherapeutic agent in 1964 but shelved because of its extreme toxicity, is a DNA chain terminator, which means that it brings DNA synthesis to a halt. It is therefore an extremely efficient cell killer. HIV is a retrovirus, and as such replicates itself by inserting its genes into a cell's genome so that when the cell divides a new copy of the virus is produced. AZT prevents the replication of HIV by killing infected T-cells; unfortunately, it kills all dividing cells indiscriminately, whether they are infected with a retrovirus or not, and will very quickly decimate even a healthy person's immune system. AZT's manufacturer, GlaxoSmith Kline, chose not to comment for this article.*

nied the standard scientific "right of reply" in response to personal attacks that were frequently published in that journal. Prior to 1987, Peter Duesberg never had a single grant proposal rejected by the NIH. Since 1991 he has written a total of twenty-five research proposals, every single one of which has been rejected. "They took him out, just took him right out," says Richard Strohman, an emeritus professor of biology at UC Berkeley.

And what was it, exactly, that Peter Duesberg had done? He simply pointed out that no one had yet proven that HIV is capable of causing a single disease, much less the twenty-five diseases that are now part of the clinical definition of AIDS.[12] He pointed to a number of paradoxes regarding HIV and argued that far from being evidence that HIV is "mysterious" or "enigmatic," these paradoxes were evidence that HIV is a passenger virus.

The classical tests of whether or not a microorganism is the cause of infectious disease are known as Koch's postulates. They state: 1) the microorganism must be found in all cases of the disease; 2) it must be isolated from the host and grown in pure culture; 3) it must reproduce the original disease when introduced into a susceptible host; and 4) it must be found present in the experimental host so infected. Although claims to the contrary have been made, Duesberg maintains that it has never been demonstrated that HIV satisfies all of Koch's postulates. His exhaustive analysis of the peer-reviewed scientific literature has revealed more than 4,000 documented AIDS cases in which there is no trace of HIV or HIV antibodies. This number is significant, because there are strong institutional forces deterring such descriptions and because the vast majority of AIDS cases are never described in formal scientific papers. In fact, most AIDS patients have no active HIV in their systems, because the virus has been neutralized by antibodies. (With all other viral diseases, by the way, the presence of antibodies signals *immunity* from the disease. Why this is not the case with HIV has never been demonstrated.) Generally speaking, HIV can be isolated only by "reactivating" latent copies of the virus, and then only with extraordinary difficulty. Viral load, one of the clinical markers for HIV, is not a measurement of actual, live virus in the body but the amplified fragments of DNA left over from an infection that has been suppressed by antibodies. Another embarrassment for the HIV hypothesis is the extraordinary latency period between infection and the onset of disease, despite the fact that HIV is biochemically most active within weeks of initial infection. This la-

[12] *HIV was declared the probable cause of AIDS in a U.S. government press conference in 1984. It was claimed that the virus had been discovered by NIH researcher Robert Gallo. In fact, Gallo had not discovered HTLV-III (Human T-cell Lymphotropic Virus III, as it was known before it was rechristened with the more memorable name HIV). That honor belongs primarily to Luc Montagnier, of the Pasteur Institute, who had sent Gallo a sample of the virus.*

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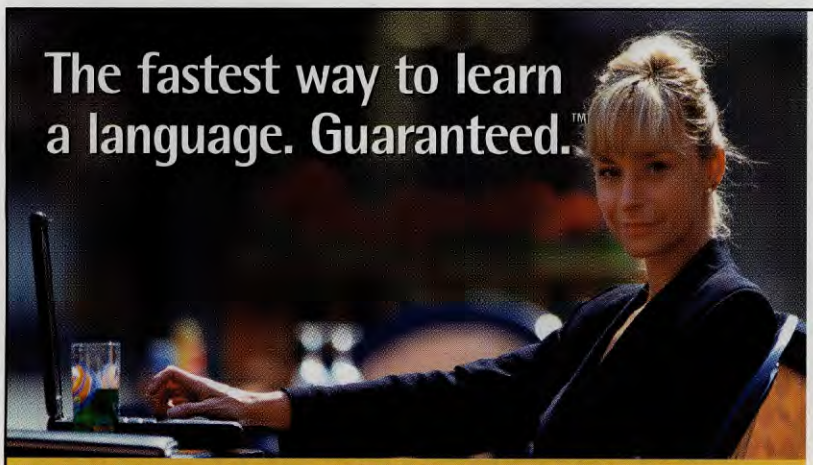

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tency period, which apparently grows with every passing year, enables proponents of the theory to evade Koch's third and fourth postulates.

The foregoing is merely a sketch of the central mystery presented by the HIV theory of AIDS. There are many more, which Duesberg has laid out very carefully in his scientific papers and in a trade book published ten years ago, but they all boil down to the central point that when it comes to AIDS, basic scientific standards seem no longer to apply.[13] AIDS is a "syndrome" defined by twenty-five diseases, all of which exist independently of HIV. No one has ever demonstrated the cell-killing mechanism by which HIV is supposed to cause all these different diseases, and no one has ever demonstrated how a sexually transmitted virus can manage to restrict itself overwhelmingly to gay men and other AIDS risk groups instead of spreading randomly through the population, as do all other infectious diseases. The "overwhelming" character of the evidence for HIV's causation has always been epidemiological; which is to say, a correlation, a coincidence. Whenever we have AIDS, researchers say, we also have HIV. But this correlation is a result of the official definition of AIDS, which states that a disease counts as AIDS only if it corresponds with HIV antibodies. ("AIDS without HIV" has been given a singularly unmemorable name: idiopathic CD4 lymphocytopenia.)

Given that the evidence for HIV is coincidental, a number of research avenues suggest themselves, yet orthodox AIDS researchers have failed to demonstrate, using large-scale controlled studies, that the incidence of AIDS-defining diseases is higher among individuals infected with HIV than among the general uninfected population. Consequently, it could very well be the case that HIV is a harmless passenger virus that infects a small percentage of the population and is spread primarily from mother to child, though at a relatively low rate. (This hypothesis would tend to explain the fact that the estimated number of HIV-positive Americans has remained constant at about 1 million since 1985.) Nor have large-scale controlled studies been carried out to directly test the AIDS-drug hypothesis, which holds that many cases of AIDS are the consequence of heavy drug use, both recreational (poppers, cocaine, methamphetamines, etc.) and medical (AZT, etc.).[14] Nor have controlled studies been carried out to prove that hemophiliacs infected with HIV die sooner than those who are not infected. Such studies might be expensive and tedious, but expense has never been a serious objection to AIDS researchers, who have spent many billions of dollars in the last twenty years on HIV research and practically nothing on alternative causes or even co-factors. (Even Luc Montagnier, the discoverer of HIV, has stated repeatedly that the virus cannot cause AIDS without contributing causes.)

Attempts to rigorously test the ruling medical hypothesis of the age are met not with reasoned debate but with the rhetoric of moral blackmail: *Peter Duesberg has the blood of African AIDS babies on his hands. Duesberg is evil, a scientific psychopath. He should be imprisoned.* Those who wish to engage the AIDS research establishment in the sort of causality debate that is carried on in most other branches of scientific endeavor are tarred as AIDS "denialists," as if skepticism about the pathogenicity of a retrovirus were the moral equivalent of denying that the Nazis slaughtered 6 million Jews. Moral zeal rather than scientific skepticism defines the field. It has been decided in advance that HIV causes AIDS; consequently all research and all funding must proceed from that assumption. Similarly, it was known in advance that AZT was a "magic bullet" against HIV; the word was out that it was a "life-saving drug" before anyone could possibly verify this, and so scientific controls were compromised. Journalists (myself included) who reported at the time that the drug apparently was killing patients were labeled "AZT refuseniks" and even "murderers."

The nevirapine debate follows the same histrionic, antiscientific pattern. Because of his concerns about the toxicity of this and other antiretroviral drugs, President Thabo Mbeki of South Africa was pilloried in the international press as pharmaceutical companies and their well-funded "activist" ambassadors repeated their mantra about "life-saving drugs." So, too, was Jonathan Fishbein, who never questioned the premise that HIV causes AIDS, tarred and feathered for pointing out that the NIH flagship study on nevirapine was a complete disaster. Fishbein's failure to fall into line, his failure to understand in advance of experimental proof that nevirapine was too important to fail, meant that the AIDS bureaucracy's neutralizing antibodies had to be activated to destroy them.

In the end, the NIH failed to si-

[13] *It has been claimed that HIV somehow causes cell death even when it is not present by remote programmed "suicidal" mechanisms. Some researchers claim that HIV exploits special receptors on human T-cells that, due to a hypothetical genetic mutation, many "Caucasian Europeans" lack, but most Africans have. What's interesting is that many gay men also seem to possess these mysterious receptors, as do intravenous drug users and transfusion recipients.*

It is claimed that although HIV does not kill the laboratory T-cells used to manufacture AIDS tests, it does kill T-cells in the human body, even though it infects only a very small proportion of them, typically an average of 0.1 percent. HIV does not sicken or kill chimpanzees, though they do produce antibodies. It was recently claimed that HIV appears to be evolving into a form less dangerous to human beings. Such unproven hypotheses about the ingenuity of HIV proliferate in the popular and scientific media like the seasonal flu. Seldom do journalists insist on good hard evidence for these assertions.

[14] *There is ample statistical and epidemiological evidence linking the rise of mass drug abuse in the late Sixties and Seventies with the sudden appearance of AIDS. The overwhelming majority of AIDS patients with Karposi's sarcoma, for example, have been heavy users of nitrate inhalers, or "poppers." The case of "super AIDS" that was recently reported in New York turned out upon closer examination to be an individual with an extraordinarily heavy methamphetamine habit.*

lence Fishbein. In late December 2005, he won his case and was retroactively reinstated at the agency, though he won't be returning to DAIDS. He is unable to discuss the terms of his settlement, but he has promised to continue his commitment to research integrity and the protection of human research subjects. Peter Duesberg has been less successful, though there are signs of rehabilitation.

Regardless of whether Duesberg is right about HIV, his case, like Fishbein's, lays bare the political machinery of American science, and reveals its reflexive hostility to ideas that challenge the dominant paradigm. Such hostility is not unusual in the history of science,[15] but the contemporary situation is dramatically different from those faced by maverick scientists in the past. Today's scientists are almost wholly dependent upon the goodwill of government researchers and powerful peer-review boards, who control a financial network binding together the National Institutes of Health, academia, and the biotech and pharmaceutical industries. Many scientists live in fear of losing their funding. "Nobody is safe," one NIH-funded researcher told me. "The scientific-medical complex is a $2 trillion industry," says former drug developer Dr. David Rasnick, who now works on nutrition-based AIDS programs in Pretoria, South Africa. "You can buy a tremendous amount of consensus for that kind of money."

"You have to write a grant a year almost. And you have to write four to get one, if you're any good. I got out just in time. Everybody who's still in there says the same thing," says Berkeley's Strohman. "Before the biotech boom, we never had this incessant urging to produce something useful, meaning profitable. Everybody is caught up in it. Grants, millions of dollars flowing into laboratories, careers and stars being made. The only way to be a successful scientist today is to follow consensus. If you're going to produce something and put it on the market you don't want any goddamn surprises. You've got the next quarter to report and you don't want any bad news. It's all about the short term now. Science has totally capitulated to corporate interests. Given their power and money, it's going to be very hard to work our way out of this."

Duesberg has never been afraid to challenge consensus, but contrary to what many in the AIDS establishment would have us believe, he is very far from being a scientific psychopath.[16] In 1997, on the brink

[15] *Few today remember the controversies over scurvy and pellagra, which, until the discovery of vitamin C and niacin, were blamed by the medical establishment on mysterious infectious agents. Those who pointed out, even before they knew the cause, that dietary changes cured both conditions were dismissed as flat-earthers.*

[16] *Nor is Duesberg alone in dissenting from AIDS orthodoxy. More than 2,300 people, mostly scientists and doctors, including Nobelists in chemistry and medicine, have signed the petition of the Group for the Scientific Reappraisal of the HIV-AIDS Hypothesis, which calls for a more independent and skeptical approach to the question of AIDS causality.*

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of scientific demise in the U.S., Duesberg was quietly invited back to his native Germany to resume his cancer research. During this time, commuting biannually between Mannheim and Berkeley, Duesberg formulated and tested a theory that shifts the focus of cancer causation from the "mutant gene" theory that has reigned for about three decades to a simpler explanation that revives ar abandoned thread of research from early in the twentieth century, which posited that cancer is caused by chromosomal malfunction, now known as "aneuploidy."

Harvey Bialy, the founding scientific editor of *Nature Biotechnology*, a sister journal to *Nature*, recently spent four years writing a scientific biography of Duesberg entitled *Oncogenes, Aneuploidy, and AIDS*. The book is a history of the papers, review articles, and letters that Duesberg published between 1983 and 2003, and the responses they generated. I asked him why he wrote the book. "I am persuaded that aneuploidy is the initiating event in carcinogenesis," Bialy said. "Peter has found the genetic basis for cancer. The most immediate application of it will be early diagnosis."

"When aneuploidy, or genetic instability, or whatever linguistic term you want to use, gets reincarnated as the dominant theoretical explanation for the genesis of cancer, Peter Duesberg will be recognized as a major contributor to that," Bialy said. "I wanted to make sure that his contributions were not swept aside or ignored." I asked him about the AIDS controversy. "AIDS is a political thing, and Peter's stuck in it. There's nothing to discuss anymore on that." Bialy made a critical point: Science is amoral and should be. There is no right and wrong, only correct and incorrect. "Duesberg," Bialy said, "is a *classical* molecular biologist. All he is interested in is rigorously testing dueling hypotheses. The twin pillars, AIDS and oncogenes, both are crumbling because of the questions Peter Duesberg put into motion."

"The basis of speciation is changing the content and the number of chromosomes," says Duesberg. "Cancer is essentially a failed speciation. It's not mutation. Cancer is a *species*. A really bad breast, lung, or prostate cancer has seventy, eighty, or more chromosomes. Those are the real bad guys—they're way outside our species. But it's a rare kind of species that as a parasite is more successful in its host than the normal host cell is."

There has been considerable international interest in Duesberg's new research.[17] In January 2004, he hosted a conference on aneuploidy and invited fifty cancer researchers from around the world who also have been working on the connections between aneuploidy and cancer. Seventy showed up, including such luminaries as Thomas Ried, the National Cancer Institute's head of cancer genomics, Gert Auer from the Karolinska Institute in Stockholm, and Walter Giaretti, who heads the equivalent of the NCI in Italy. And on May 31 of last year, amid considerable tension, Duesberg was invited by the National Cancer Institute to give a talk at the NIH. The auditorium crackled with nervous tension as people filed in and took their seats. His talk was succinct and laced with his characteristic irony, but the questions afterward were civilized, with no tangible hostility. All was not forgiven, however. After the talk, while Duesberg remained at the podium talking to a group of people from the audience, I noticed a very angry-looking NIH publicist standing at the back of the room admonishing a colleague, a scientist, who'd posed a question that somehow connected aneuploidy to HIV. "*You opened it up*," she scolded. "We got through it okay, but you *opened it up*." As the questioner tried to defend himself, a thickset man who'd been standing in the circle said loudly, as though intending to broadcast it across the room: "Well, at least if he's wrong about this he won't be *killing millions of people*."

Nobel laureate Kary Mullis, who discovered the revolutionary DNA technique called the polymerase chain reaction, has long been a supporter of Duesberg, but he has grown weary of the AIDS wars and the political attacks on contrarian scientists. "Look, there's no sociological mystery here," he told me. "It's just people's income and position being threatened by the things Peter Duesberg is saying. That's why they're so nasty. In the AIDS field, there is a widespread neurosis among scientists, but the frenzy with which people approach the HIV debate has slacked off, because there's just so much slowly accumulating evidence against them. It's really hard for them to deal with it. They made a really big mistake and they're not ever going to fix it. They're still poisoning people."

Duesberg thinks that up to 75 percent of AIDS cases in the West can be attributed to drug toxicity. If toxic AIDS therapies were discontinued, he says, thousands of lives could be saved virtually overnight. And when it comes to Africa, he agrees with those who argue that AIDS in Africa is best understood as an umbrella term for a number of old diseases, formerly known by other names, that currently do not command high rates of international aid. The money spent on antiretroviral drugs would be better spent on sanitation and improving access to safe drinking water (the absence of which kills 1.4 million children a year).

It's too late to save people like Joyce Ann Hafford, but it is possible that an open and honest debate about the risks of current AIDS treatments and the scientific questions concerning HIV could save others. ■

[17] *Even so, the National Cancer Institute still refuses to fund him. Duesberg has submitted five grant proposals to study aneuploidy, and all have been rejected. One of the most influential cancer researchers in the country, Bert Vogelstein, Clayton Professor of Oncology and Pathology at Johns Hopkins University, has written a letter urging the NCI to reconsider. "I agree with him that aneuploidy is an essential part of cancer," Vogelstein wrote. "Dr. Duesberg continues to have a major impact on this burgeoning area of research, through his careful experimental observations as well as through his thoughtful reviews and critiques of the subject. There is no question that he is a world leader in this field of investigation."*